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EXAMINER	
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ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/992,994	RASO, VICTOR	
	Examiner	Art Unit	
	STACEY MACFARLANE	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *85 and 86* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *85 and 86* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claims 85 and 86 are pending in the instant application and are under examination in the instant office action.

Claim Objections

2. Claims 85 and 86 are objected to because of the following informalities: See MPEP section 608.01(m), "Each claim begins with a capital letter and ends with a period. Periods may not be used elsewhere in the claims except for abbreviations. See Fressola v. Manbeck, 36 USPQ2d 1211 (D.D.C. 1995)". Specifically the claims contain periods between "NO" and ":". Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 85 and 86 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an in vitro method for forming and detecting an immune complex, does not reasonably provide enablement for the method wherein steps (a) through (c) occur in vivo. The specification does

not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

5. Claims 85 and 86 are drawn to a method for forming and detecting an immune complex comprising:

a) providing beta-amyloid in the presence of physiological levels or 60 mg/ml of human serum albumin;

b) forming an incubation mixture comprising the components of step a) and an antibody generated to the central region of beta-amyloid SEQ ID NO: 3;

c) incubating the mixture of step b) under conditions appropriate for the binding of antibody to antigen to form an incubation mixture the immune complex; and

d) removing a sample from the incubation mixture of step c) and detecting the immune complex of beta-amyloid and an antibody generated to the central region of beta- amyloid SEQ ID NO: 3 in the presence of physiological levels of human serum albumin.

6. The “central region”, as defined as SEQ ID NO: 3 within the claims, comprises residues 9-25 of the beta-amyloid peptide.

7. The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of

the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. In re Wands, 8 USPQ2d, 1400 (CAFC 1988).

8. With respect to claim breadth, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. In addition, when analyzing the scope of enablement, the claims are analyzed with respect to the teachings of the specification and are to be "given their broadest reasonable interpretation consistent with the specification." See MPEP 2111 [R-5]; Phillips v. AWH Corp., 415 F.3d 1303, 75 USPQ2d 1321 (Fed. Cir. 2005); and In re Hyatt, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). Applicant always has the opportunity to amend the claims during prosecution, and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be interpreted more broadly than is justified. In re Prater, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550- 51 (CCPA 1969).

9. As such, the broadest reasonable interpretation of the claimed method is that it can either be performed by forming an incubation mixture comprising beta amyloid (Aβ), physiological levels of human serum and an antibody against SEQ ID NO: 3 in vitro; OR it can be performed by active immunization of a beta amyloid peptide comprising SEQ ID NO: 3 to a human subject and removing a serum sample from said subject to detect the immune complex.

10. As opposed to the claims, what is disclosed about the claimed method is narrow: Pages 26-28 of the specification teach immunization of mice and

generation of a monoclonal antibody raised against a Phenylalanine-statine transition state KLH - Aβ10-25 peptide conjugate (Specification pages 27, line 2, page 36 lines 24-32, and Table 8). The specification teaches the generation of 30 antibodies and states on page 26, "the ability of purified 5A11 monoclonal anti-Aβ antibody to bind 125I-Aβ1-40 was unaffected by the presence of human serum albumin (HSA) at 60 mg/ml, even though this was a 500-fold molar excess over the antibody concentration (Table 3)". There is no guidance within the specification as to how the method would be performed in vivo in a human with a reasonable expectation of success. While the method provides in vivo guidance for administration of an amyloid beta peptide (125I-Aβ1-40) concomitantly with the anti-Aβ antibody 5A11 (Specification page 31 lines 19-31), this method is performed in mice. It is well-recognized in the art that mice have lower physiological levels of serum albumin (36-46 mg/ml), thus the method as disclosed in the specification does not occur in the presence of physiological levels or 60mg/ml of human serum albumin. Furthermore, there is no guidance or direction within the instant specification for step (d) of the instant claims, comprising removing a sample and detecting an immune complex between the antibody and the Aβ peptide. Additionally, there is no guidance for the method as performed in humans in vivo. Absent such guidance one would rely upon what was known in the art at the time of filing regarding the method performed in humans in vivo.

11. Methods comprising administration of beta amyloid for the treatment of Alzheimer's disease are not new and were first described by Kline and

McMichael in US Patent application published in 1991. The Schenk et al. (1999), art, cited in previous Office actions, describes the production of antibodies following active immunization with an Aβ peptide and describes treatment of Alzheimer's disease in humans. Since the method that Schenk describes occur in vivo, the resultant immune complex would necessarily be formed in the presence of physiological levels of human serum albumin. However, Schenk et al. do not explicitly teach or suggest the removal of a sample to detect the immune complex of amyloid beta and an antibody raised against the central portion, as required by step (d) of the instant claims. In fact, although human clinical trails for the Schenk method began in December 1999, there was nothing within the art to teach or suggest detection of an immune complex formed between following administration Aβ antigen and the resultant auto-antibody in undiluted serum from immunized patients. There is some suggestion for step (d) of the claims as performed in humans within the post-filing literature (Hock et al., Nature Medicine, 8(11):1270-1275, 2002), however, epitope mapping of these antibodies generated from active immunization against Aβ reveal that they are all generated to the N-terminal of the peptide and not the central region as required by the claims (Lee et al., Ann Neurol, 58: 430-435, 2005). Thus, at the time of filing unpredictability remained with respect to the ability of the in vivo embodiment of the claimed invention, comprising providing a human subject with a beta amyloid peptide in the presence of physiological levels of human serum albumin, to successfully form an antibody against the epitope SEQ ID NO: 3, and to allow for detection of the immune complex in a serum samples.

12. Since there is no specific guidance for the method as performed in humans in vivo either in the instant disclosure or the art of record, then one of ordinary skill in the art would have had to make a substantial inventive contribution in order to successfully practice the method commensurate in scope with the claims.

13. The instant specification is not enabling because one cannot follow the guidance presented therein, or within the art at the time of filing, and practice the claimed method without further experimentation. A skilled artisan would have had to perform a clinical trail by actively immunizing human subjects comprising providing said subjects with a beta amyloid peptide, demonstrating that an antibody against the central region of the peptide could be successfully generated, and then detecting the resultant immune complex in a serum sample removed from the subject. Such experimentation goes beyond, that which is considered routine in the art, and constitutes undue further experimentation in order to enable the invention commensurate in scope with the claims.

14. The standard of an enabling disclosure is not the ability to make and test if the invention works but one of the ability to make and use with a reasonable expectation of success. A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of Genentech, Inc, v. Novo Nordisk, 42 USPQ 2d 1001, (CAFC 1997), the court held that:

"[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and

that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

15. Therefore, Claims 85 and 86 are rejected under 35 U.S.C. 112, first paragraph, for failing to meet the enablement requirement.

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

17. Claims 85 and 86 are rejected under 35 U.S.C. 102(b) as being anticipated by Cordell et al., US Patent 5,187,153 (1993), as evidenced by the reference from the Australian Proteome Analysis Facility, submitted as Exhibit A

in Remarks filed 6/13/2008, and Crowther, ELISA: Theory and Practice, Methods in Molecular Biology 42, Humana Press, Totowa, NJ, May 1, 1995.

18. Claims 85 and 85 are drawn in part to an in vitro method for forming and detecting an immune complex comprising:

a) providing beta-amyloid in the presence of physiological levels or 60 mg/ml of human serum albumin;

b) forming an incubation mixture comprising the components of step a) and an antibody generated to the central region of beta-amyloid SEQ ID NO.: 3;

c) incubating the mixture of step b) under conditions appropriate for the binding of antibody to antigen to form an incubation mixture the immune complex; and

d) removing a sample from the incubation mixture of step c) and detecting the immune complex of beta-amyloid and an antibody generated to the central region of beta- amyloid SEQ ID NO.: 3 in the presence of physiological levels of human serum albumin.

19. The Australian Proteome Analysis Facility reference provided by Applicant s relied upon as evidence that physiological serum human albumin is ~60mg/ml.

20. SEQ ID NO: 3 of the instant claims consists of residues 9-25 of the beta-amyloid peptide

21. Applicant has traversed this rejection on the grounds that the formation of an immune complex in the presence of physiological levels of human serum albumin is not taught within the Cordell reference. On pages 4-5 of Remarks filed 12/22/2010, Applicant argues that ELISA assays typically required the

dilution of the sample to be tested buts the concentration of serum Albumin in the ELISA cannot be physiological.

22. While this has been considered in full, it is not found to be persuasive for the following reasons. Firstly, the presence of physiological levels of human serum albumin pertains only to the method step where the antibody is "generated" and not for the detection step. Claims are drawn to a forming a mixture comprising beta amyloid, antibody and physiological albumin; forming an immune complex between antibody and antigen; and removing a sample from that incubation mixture for detection of said immune complex. Applicant's own methods in the disclosure teach binding in the presence of serum albumin (Specification page 26, at line 5) but the ELISA detection methods described require dilution of serum (page 25) and hence do not require physiological serum levels.

23. Cordell et al. teach detection of the "presence of immunoreactive serum proteins … by standard immunoassay techniques, such as solid-phase ELISA techniques" (Column 13, lines 8-10) and says nothing regarding the dilution of serum. Specifically, the Cordell et al. Patent teaches an in vitro method of diagnosing familial amyloidosis or Alzheimer's disease by detecting amyloid beta and fragments thereof that circulate in the serum at a level differentiable in Alzheimer's victims relative to unafflicted individuals (column 3, lines 22-25). Cordell et al. describe a method comprising removing a serum sample from a patient, and analyzing immunoreactivity of beta amyloid related proteins in the serum with a "panel of antibodies which are specific against peptides derived

from different regions" of beta amyloid (column 11, lines 60-68). Since the beta amyloid peptides are within the serum sample taken from the patient, they necessarily were generated in the presence of, and the serum comprises, physiological levels of human serum albumin. Futhermore, the Cordell reference does not specifically state that the serum is diluted before reaction with the antibodies (column 13, lines 1-34), and the instant claims do not specifically require the presence of albumin during detection. It is inherent that the serum sample contains beta amyloid and since the sample is drawn from the patient it inherently The Cordell Patent specifically discloses antibodies raised against the "beta amyloid core protein" were known in the art (column 2, lines 5-57), and specifically discloses antibodies binding to residues 1-10 and 8-17 within the SEQ ID NO:3 required by the claims.

24. Additionally, the Crowther reference is relied upon as evidence that it was well-recognized within the art that whole serum can be used in solid-phase ELISA (See page 169). Thus, even though the claims do not specifically require undiluted human serum, such methods were known at the time of filing.

25. Thus, the method of the instant invention fails to distinguish over the in vitro methods known in the prior art.

26. The rejection of Claims 85 and 86 under 35 U.S.C. 102(a) as being anticipated by Schenk et al. WO99/27944 published June 10, 1999, 6 days before the effective filing date of the instant application, is withdrawn. The

Declaration under 37 CFR 1.132 filed Victor Raso is sufficient to overcome the rejection of claims 85 and 86 based upon the Schenk reference.

Conclusion

27. No Claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACEY MACFARLANE whose telephone number is (571)270-3057. The examiner can normally be reached on M-R 5:45 to 3:30, TELEWORK-Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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